utilizing a very low calorie diet (420 kcal/day) for a similar period of time. Amatruda and coworkers, in contrast, reported an 8% reduction of body weight in obese NIDDM subjects of which less than 50% can be assumed to be fat under these conditions. Furthermore, Kanders et al reported an average body weight loss of 2.3 pounds per week in nondiabetic obese females subjected to similar very low calorie diets. This also amounts to a reduction of about one pound of fat per week under these restricted calorie conditions, which is less than the fat loss of 1.4 pounds per week average achieved with bromocriptine treatment in the present study.

The reduction of body fat produced by bromocriptine treatment differs in a significant way from reduction of fat achieved by caloric restriction. With very low calorie diets only about 45% of the weight loss is lipid; the remainder includes protein, carbohydrate and water.

The data show that metabolic states are regulated at least in part by an interaction of circadian neuroendocrine rhythms. This hypothesis proposes that the daily rhythms of cortisol and prolactin are individual expressions of two separate circadian systems and that the daily injections of these hormones can reset the phase relations of these two systems. Thus, in a hamster model it has been found that the 0-hour relation resets the circadian oscillations into a pattern that maintains the lean, insulin sensitive state and the 12-hour relation permits retention of a pattern that maintains the obese, insulin resistant state. Another important addition of the present study is that the effects of timed injections of a dopamine agonist, or prolactin inhibiting compound, are long lasting. Apparently once reset, the phase relation of the two circadian oscillations tends to maintain its altered pattern.

Changes in the phase relations of two circadian neuroendocrine oscillations are evidenced by changes in the phase relations of their circadian expressions. This expectation is fulfilled respecting plasma glucocorticosteroid and prolactin rhythms. In several species examined, the phase relations of the two hormone rhythms differ in lean and fat animals.

The phase relation between the circadian rhythm of plasma insulin concentration and the rhythm of lipogenic responsiveness to insulin is shown to differ in lean and fat animals. Whereas the daily interval of lipogenic responsiveness remains near light onset, the phase of the insulin rhythm varies markedly. The peak concentration of insulin, e.g., occurs near light onset in obese female hamsters held on short day-lengths. That is, the daily peaks of the lipogenic stimulus (i.e., insulin) and the lipogenic response to insulin coincide in fat animals and not in lean animals.

The phase relations of both prolactin and insulin rhythms as well as the rhythms of tissue responses to the hormones are important elements in the regulation of lipogenesis. All of these rhythms, then, would be phase adjusted to regulate lipogenesis. Phase adjustment of these and perhaps other rhythms may also account for insulin resistance.

It is apparent that various modifications and changes can be made without departing the spirit and scope of this invention.

Having described the invention, what is claimed is:

1. A method for modifying or regulating glucose metabolism in an animal or human subject in need of such treatment comprising

administering to said subject a prolactin-inhibiting compound on a timed daily basis in a dosage amount and for a period sufficient to achieve in said subject at least one of the following modifications: decrease in insulin resistance, reduction of hyperinsulinemia, increase in glucose tolerance, and reduction of hyperglycemia.

2. The method of claim **1** wherein the prolactin-inhibiting compound is a dopamine agonist.

3. The method of claim **2** wherein at least one of said modifications persists for at least one month after cessation of administration of said dopamine agonist.

4. The method of claim **2** wherein the dopamine agonist is administered once a day, and said dosage amount is within the range from about 3 micrograms to about 100 micrograms per pound of body weight of said subject.

5. The method of claim **4** wherein the dopamine agonist is administered for a period of time within the range of from about 10 to about 150 days.

6. The method of claim **2** wherein said subject is a human and the dopamine agonist is administered once a day, and said dosage amount is within the range from about 3 micrograms to about 100 micrograms per pound body weight of said subject.

7. The method of claim **6** wherein the dopamine agonist is administered for a period of time within the range from about 30 days to about 150 days.

8. The method of claim **6** wherein said human subject exhibits at least one of insulin resistance and Type II diabetes and the dopamine agonist is administered once a day, at a time from 1 hour to about 10 hours after the time at which the prolactin bloodstream level peaks in a lean, insulin sensitive human.

9. The method of claim **2** wherein the compound is selected from the group consisting of 6-methyl-8-beta-carbobenzyloxy-aminoethyl-10 alpha-ergoline; 1,6-dimethyl-8-beta-carbobenzyloxy-aminoethyl-10 alpha-ergoline; 8-acylaminoergolenes; ergocornine; 9,10-dihydroergocornine; bromocriptine, and D-2-halo-6-alkyl-8-substituted ergolines.

10. The method of any one of claims **1–9** wherein the compound is bromocriptine.

11. A method for modifying or resetting the prolactin rhythm of an insulin insensitive or diabetic animal or human subject which comprises

administering to said subject a prolactin-inhibiting compound once a day, at a predetermined time within a 24-hour period, in an amount sufficient, and for a period of time sufficient to accomplish at least one of the following: decrease insulin resistance, decrease hyperglycemia, decrease hyperinsulinemia in said subject, and increase glucose tolerance..

12. A method for modifying or resetting the prolactin rhythm of an insulin insensitive or diabetic animal or human subject comprising

administering to said subject a prolactin-inhibiting compound on a timed daily basis at a time of day designed to cause the daytime prolactin bloodstream level of said subject to decrease at a time corresponding to the low daytime prolactin level of a lean, insulin sensitive subject, in a dosage amount sufficient and for a period of time sufficient to achieve in said subject at least one of the following modifications in glucose metabolism: decrease in insulin resistance, reduction of hyperinsulinemia, improvement in glucose tolerance and reduction of hyperglycemia.

13. The method of claim **12** wherein the prolactin-inhibiting compound is a dopamine agonist.

14. The method of claim **12** wherein said dosage amount is within the range of about 3 to about 100 micrograms per pound of body weight of said subject.

15. The method of claim **14** wherein on cessation of